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09/295,691	04/21/1999	JON FAIZ KAYYEM	A-67465/RFT/	7483

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DORSEY & WHITNEY LLP
Four Embarcadero Center
Suite 3400
San Francisco, CA 94111-4187

EXAMINER	
STARSIAK, JOHN S	

ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/295,691	KAYYEM, JON FAIZ	
	Examiner	Art Unit	
	John S. Starsiak Jr.	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-39,45-50 and 52-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-39,45-50 and 52-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *022204*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 39 and 45 are objected to because of the following informalities: Claim 39 recites "a filter ... positioned between said sample handling well and said second microchannel". This recitation conflicts with the written description of the invention, i.e. "as shown in Fig. 1B where filter 200 is between the handling well 40 and detection well 30...". In Fig. 1B filter 200 is illustrated as being in the second microchannel. Claim 45 appears to correspond to embodiments of the invention illustrated in Fig. 1D and 2F. In these embodiments these is no "second microchannel formed in said support member and extending between said sample handling well and said detection well for the flow of said fluid sample there between" (recited in claim 36, upon which claim 45 depends). Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36-39, 45, 46, 49, 50, 53, and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilding et al in view of Bamdad.

Wilding et al discloses mesoscale polynucleotide devices comprising: a solid support member (solid substrate 14); a sample holding module including a sample handling well formed in said support member (reaction chamber 22A of the device illustrated in FIG. 11); a sample inlet port (inlet/outlet port 16A of the device illustrated in FIG. 11; a first microchannel (mesoscale flow channel 20A of the device illustrated in FIG. 11) formed in said support member coupled to and extending between said sample handling well and said sample inlet port; a detection well formed in said substrate (detection chamber 22B in the device illustrated in FIG. 11); and a second microchannel (mesoscale flow channel 20B of the device illustrated FIG. 11). The only difference between the device of Wilding et al. and claim 36 is the detection means in the detection well/chamber is different. However, Wilding et al. teaches [col. 19, lines 5-15]: "The presence of amplified polynucleotide disposed either in the substrate or in the appliance can be detected by any number of methods including, *but not limited to*: (1) monitoring the pressure or electrical conductivity of sample fluids entering and/or exiting the reaction chamber in the mesoscale flow system; (2) forming a detectable complex by, e.g., binding the polynucleotide product with a labeled probe, such as a labeled oligonucleotide or antibody probe; and (3) electrophoretically separating the polynucletide product from reactants and other components of the sample." Wilding et al. teach additional means for detection in section F. Detection of Amplified Polynucleotide. Hence, it is clear that any known means for detecting polynucleotides

can be used in the devices of Wilding et al. Bamdad discloses a means for detecting DNA molecules which includes the particulars recited in claim 36. For example, the embodiment illustrated in FIG. 11 comprises: an electrode 22/26, a self-assembled monolayer 28 and a binding ligand 34. Bamdad teaches the disclosed structure can be incorporated into microfluidic devices, i.e., [column 17, lines 41-44]: "It will be understood that the procedure given in the examples for the preparation of a DNA chip may be applied to the preparation of any DNA chip...". It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the detection means of Bamdad for the detection means of Wilding et al. because Wilding et al. indicates that the any known DNA detection means can be utilized in their devices. The only difference between claim 36 and claim 55 is that claim 36 recites "a sample handling module including a sample handling well formed in said support member to receive and store said sample" and claim 55 recites "a reaction module formed in said support member". Since the reaction module of claim 55 also reads on "reaction chamber 22A" of Wilding et al, the above rejection of claim 36 also applies to claim 55. Regarding the limitation recited in claims 49 and 50 Wilding et al teaches [column 16, lines 43-46]: "A pump 53 in appliance 50 is used to deliver a sample and/or reagents from flow line 56 in the appliance to the reaction chamber 22 via the inlet ports 16." Regarding the recitation of and "electron transfer moiety" claims 54 and 56, while Bamdad does not explicitly recite an "electron transfer moiety" this particular is considered to be inherent in Bamdad because Bamdad teaches that electron transfer occurs in the device. For example, Bamdad teaches [column 10, lines 47-49]: "The

present invention provides for a technique for molecular recognition at surfaces that involves *electron transfer* through a biological species immobilized at the surface." The embodiment of Wilding et al. illustrated in Fig.12 comprises: a solid support (substrate 14); s sample handling module (cell lysis chamber 22B); a sample inlet port (entry/exit port 16A); a detection well (restricted flow detection region 40); a reaction module (PCR reaction chamber 22C/22D) positioned between said sample handling module and said detection well; a filter 24 between said sample handling module and the detection well; and microchannels interconnecting said inlet, said sample handling module, said reaction module, and said detection well. The only difference between claims 39 and 49 and this embodiment of Wilding et al. is the detector structure. It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the detector of Bamdad for the detector structure of Wilding et al. because of the reason(s) recited above. Regarding claims 37 and 38, while Fig.12 illustrates membrane piercing protrusions 90 in chamber 22B Wilding teaches [column 22, lines 55 & 56]: "Cell lysing agents known in the art can be utilized." Regarding claim 46, Wilding teaches [column 26, lines 16-25]: "The amplification of a sample polynucleotide,...in a mesoscale reaction chamber...To conduct the reaction, PCR reagents ... were mixed in tubes and transferred to the mesoscale reaction chamber in the silicon substrate."

Claims 36-38, 45, 46, 49, 50, and 52-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zanzucchi et al. in view of Bamdad.

Zanzucchi et al. discloses a generic microfluidic system comprising: "a device array of micron sized wells and connecting channels..." (column 2, lines 21 & 22). "each well in the array is designed so to accomplish a selected task in appropriate modules on a substrate, each module containing the number of wells required to complete the task. The wells are connected to each other, to a sample source and to a source of reagent fluids by means of connecting microchannels." (column 2, lines 48-54). Zanzucchi et al. discloses a module 48 illustrated in FIG. 1B comprising a disk 14 with a loading channels 34 and 50, four wells 36, 40, 42, 44, and a connecting channel 38. However, Zanzucchi et al. teaches [column 6, lines 26—28]: "the module 48 illustrated in FIG. 1B comprises four connecting wells, but this is by way of example only, and more or fewer wells can be present depending on the tests or synthesis to be performed in each module...". Hence, claims 36 and 55 read on a two well embodiment of Zanzucchi et al. The solid support member recited in claims 35 and 55 reads on disc 14 of Zanzucchi et al. The sample handling module recited in claim 36 is such a broad recitation that it reads on the any first well 36 of Zanucchi et al. The sample inlet recited in claim 36 and 55 reads on either loading channel 34 or loading channel 50 of Zanzucchi et al. Zannzuchi et al. teaches [column 10, lines line 36 & 37]: "A well known means of assay DNA is the hybridization technique. The third well 42 is used for this purpose." Hybridization involves the use of a binding ligand, i.e., a DNA probe. Hence, the detection well and binding ligand recited in claim 36 and 55 read on this teaching. The first and second microchannels recited in claim 36 and 55 read on the portion of connecting channel 38. The only difference between Zanzucchi et al. and claims 36

and 55 is the details of the "detection module", i.e., an electrode and a self-assembled monolayer (SAM), recited in claims 36 and 55. Bamdad discloses a hybridization assay structure with the limitations recited in claims 36 and 55, i.e., "In another aspect, the invention provides a self-assembled monolayer-forming species including a nucleic acid strand. The nucleic acid strand can be single-stranded DNA or double stranded DNA, or another species. The nucleic acid strand can be a single nucleic acid strand free of hybridization from a complementary strand, and /or can form a part of a self-assembled monolayer of other nucleic acid strand species. The nucleic acid strand can be covalently coupled to a self-assembled monolayer-forming species, thereby forming a part of a self-assembled monolayer." Also, see the details of Bamdad cited in the previous rejection. It would have been obvious to one of ordinary skill in the art at the time of the invention that the hybridization assay structure of Bamdad could be incorporated into the microfluidic device (s) of Zanzucchi et al. because Bamdad indicates that the structure could be used in microfluidic devices. Regarding the limitations in claims 27, 28, 49, and 50 Zanzucchi et al. teaches [column 8, line 66 - column 9, line28]: "The sample fluid is passed into the loading channel 34 or loading channel 50 as explained above. The sample then moves by application of an electric field or is moved by a pump 22 into the first well 36 through the channel 38, where the separation of the sample, e.g. filtration, *lysation* and DNA separation, takes place...A white corpuscle lysis buffer solution...is then passed into the first well 36 via the channel 38 in an amount sufficient to lyse the white corpuscles." Regarding the limitation recited in claim 52, Zanzucchi et al. teaches that if the first well is used for lysing cells that a

valve should be placed in the portion of channel 38 downstream from the first well, i.e., [column 9, lines 34-39]: "Because of the high temperatures required in the last two steps, a significant vapor pressure may develop in the first well 36, causing a back pressure in both directions-back toward the sample loading channel 34 and forward to the succeeding well 40. Thus preformed valves 62 and 63 are shown in FIG. 6A,..." Regarding claim 45, this reads on the embodiment of Zanzucchi et al. except for the elements in the third well/module. Specifically, the solid support member reads on microlaboratory disk 14 of Zanzucchi et al.; the sample handling well reads on first well 36 of Zanzucchi et al.; the sample inlet port read of either channel 34 or channel 50 of Zanzucchi et al.; the reaction module reads on second well 40 of Zanzucchi et al.; the detection well reads on the third well 42 of Zanzucchi et al. Regarding the limitation recited in claim 46, Zanzucchi et al. teaches [column 10, lines 6-9]: "...the prepared and treated blood sample is then transferred to the second well 40 for *PCR amplication* of the obtained DNA sample from the first well 36." In order to use the second well of this embodiment of Zanzucchi et al. for the stated purpose, "reagents for nucleic acid acid amplification" (e.g. DNA polymerase) must be positioned in the second well of Zanzucchi et al.

Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zanzucchi et al in view of Bamdad as applied to claim 45 above, and further in view of Mullis et al.

Zanzucchi et al does nor explicitly teach providing an electrical resistance heater in the second well. However, Zanzucchi et al. does teach [column 7, lines 54-56]: " In the case where the temperature of a particular well is to be monitored or changed, a means of heating or cooling the well is built into the well,...". Also, Zanzucchi et al teaches the following structure for providing heat to a well [column 9, lines 4-14]: "The first well 36 is fitted with a means for heating and temperature control, as shown in more detail in FIG. 4. A layer of tin oxide 57 is first deposited in the well 36 by CVD. A bilayer film 59 is deposited over the tin oxide film 57 in the well 36, and a metal connection 60 is deposited along a sidewall of the well. Electrodes 56 and 60 are formed on the backside of the microlaboratory disc 14, and leads 58 and 60 connect the thermocouple 59 to the external contacts 56. The current in the leads 58 are monitored and controlled by a computer 10. It is notoriously well-known in the art the DNA amplification by PCR requires cyclic heating and cooling (thermocycling). Mullis et al. is one of thousands of references which disclose this teaching, i.e. see Abstract. It is inherent that if one of the wells of the device(s) disclosed by Zanzucchi et al. is used for PCR amplification that a resistance heater in the well is required.

Claims 36, 37, 49, 50, 53, 55, and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Segal et al in view of Wilding et al.

The "solid support member recited in claims 36 and 55 read on substrate card 20 of Segal et al. The "sample holding module" recited in claim 36 and the "reaction module" recited in claim 54 read on sample introduction zone 12 of Segal et al. The

"detection well" and the structure therein recited in claims 36 and 55 read on biosensor 32 of Segal et al. Concerning the biosensor Segal et al. teaches [Abstract]: " In another embodiment, the biosensor includes an electrode substrate coated with a high-dielectric hydrocarbon-chain monolayer, and having analyte binding agent attached to the exposed monolayer surface. Binding of analyte to the monolayer-bound analyte-binding agent, and the resultant perturbation of the monolayer structure, causes ion-mediated electron flow across the monolayer." The limitation recited in clams 54 and 56 also read on this teaching. The "second microchannel " recited in claims 36 and 55 reads on sample pathway 38 of Segal et al. The only difference between claims 36 and 55 is that Segal et al. lacks the "inlet" and "first microchannel" recited in these claims. Segal et al does not explicitly disclose any structure for introducing sample into the sample introduction region of the device. Wilding et al discloses a opening 16A and a microchannel 20A for introduction of sample in the first module/well/chamber of a microfluidic device. The "sample inlet port" and the "first microchannel" recited in claims 36 and 55 read on opening 16A and microchannel 20A of wilding et al. It would be obvious to one of ordinary skill in the art to provide the device of Segal et al with the structure of Wilding et al because it is necessary to provide means for introducing sample in order for the device of Segal et al to function. Regarding the limitations recited in claims 37, 49, 50, and 53 see previous Office actions.

Response to Arguments

Applicant's arguments with respect to claims 36-39, 45-50, 52-56 have been considered but are moot in view of the new ground(s) of rejection.

Although applicant's arguments are moot, the examiner notes that the applicant evidence fails to support the applicant's argument conception of the "claimed " subject matter. Exhibit 1 only broadly teaches combining CMS technology with microfluidic technology. Exhibit 1 does not support conception of the structure recited in the claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Starsiak Jr. whose telephone number is (571) 272-1346. The examiner can normally be reached on Monday to Friday from 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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NAM NGUYEN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1700

John S. Starsiak, Jr.

23 February 2004